Global trends in molecular epidemiology of HIV-1 during 2000–2007

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Abstract

Objective—To estimate the global and regional distribution of HIV-1 subtypes and recombinants between 2000 and 2007.

Design—Country-specific HIV-1 molecular epidemiology data were combined with estimates of the number of HIV-infected people in each country.

Method—Cross-sectional HIV-1 subtyping data were collected from 65913 samples in 109 countries between 2000 and 2007. The distribution of HIV-1 subtypes in individual countries was weighted according to the number of HIV-infected people in each country to generate estimates of regional and global HIV-1 subtype distribution for the periods 2000–2003 and 2004–2007.

Results—Analysis of the global distribution of HIV-1 subtypes and recombinants in the two time periods indicated a broadly stable distribution of HIV-1 subtypes worldwide with a notable increase in the proportion of circulating recombinant forms (CRFs), a decrease in unique recombinant forms (URFs), and an overall increase in recombinants. In 2004–2007, subtype C accounted for nearly half (48%) of all global infections, followed by subtypes A (12%) and B (11%), CRF02_AG (8%), CRF01_AE (5%), subtype G (5%) and D(2%). Subtypes F, H, J and K together cause fewer than 1% of infections worldwide. Other CRFs and URFs are each responsible for 4% of global infections, bringing the combined total of worldwide CRFs to 16% and all recombinants (CRFs plus URFs) to 20%.

Conclusions—The global and regional distributions of individual subtypes and recombinants are broadly stable, although CRFs may play an increasing role in the HIV pandemic. The global diversity of HIV-1 poses a formidable challenge to HIV vaccine development.

Keywords

HIV; subtype; Circulating Recombinant Form (CRF); recombinant; molecular epidemiology; vaccine

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Introduction

HIV-1 remains a global health problem of unprecedented dimensions, with an estimated 33.4 million people living with HIV in 2008. The pandemic is dynamic, with 2.7 million new infections and 2 million deaths occurring in 2008 [1].

HIV originated from multiple zoonotic transmissions of simian immunodeficiency virus (SIV) from non-human primates to humans in West and Central Africa in the early 1900s. HIV-1 group M, the pandemic branch of HIV, originates from SIVcpz in the chimpanzee *Pan troglodytes troglodytes* [2]. After transmission to humans, while still confined to western-central Africa, HIV-1 group M diversified into genetic subtypes (named A-D, F-H and J-K) in the first half of the 20th century [3]. HIV genetic variability is the result of the high mutation and recombination rates of the reverse transcriptase enzyme, together with high rates of virus replication. Recombinants between subtypes are designated as circulating recombinant forms (CRFs; 48 different CRFs have been described so far [4]) if fully sequenced and found in three or more epidemiologically unlinked individuals, and unique recombinant forms (URFs) if not meeting these criteria [5]. In the second half of the 20th century the global spread of HIV-1 group M took place resulting in the differential global distribution of HIV-1 subtypes and recombinants [6].

HIV diversity impacts HIV diagnosis and viral load measurements [7, 8] and may affect the response to antiretroviral treatment and the emergence of drug resistance [9, 10]. Subtypes may differ in the rate of disease progression [11–13] and some evidence suggests that subtypes are transmitted at different rates [14, 15].

HIV infection in humans induces humoral and cellular immune responses which control primary viraemia without completely eliminating infection due to the rapid selection of immune-escape mutants [16, 17]. While the induction of neutralising antibodies and effective CTL responses against HIV-1 through vaccination has proven extremely difficult, an even greater challenge is posed by the extreme genetic diversity of the virus and its continuing evolution [18].

Genetic variation within a subtype is in the order of 8–17%, whereas variation between subtypes is usually between 17–35 %, depending on the subtypes and genome regions examined [19]. This degree of diversity is likely to limit the intra- and inter-subtype cross-reactivity of immune responses [20]. To increase the likelihood of vaccine-induced immune responses cross-reacting with circulating strains, immunogens should match as closely as possible viral sequences circulating in the target population [21]. Candidate HIV vaccines tested in efficacy trials to date have been based on primary sequences of subtype B and CRF01_AE [22–24]. Recent encouraging results of a phase III HIV-1 vaccine efficacy trial in Thailand emphasise the importance of further studies on global and regional HIV diversity to inform rational vaccine design and development [24].

Data on the global distribution of HIV subtypes is limited. HIV sequences deposited in the Los Alamos sequence database are not representative for the distributions in the countries of origin [4]. Some studies have relied on pooling published data from a wide range of years, an approach which is hampered by publication bias and a lack of information on trends [25]. Here we present an analysis of the global and regional distribution of HIV-1 subtypes and recombinants for the periods 2000–2003 and 2004–2007 using a combination of cross-sectional country-specific HIV-1 molecular epidemiology data, derived from published and unpublished sources, and estimates of the number of HIV-infected people in each country.

Methods

Country-specific cross-sectional subtype distribution data

Data on the distribution of HIV-1 subtypes and recombinants in individual countries were obtained from researchers in the field and from a comprehensive literature review. Research laboratories across the globe specialising in subtyping of HIV-1 samples were solicited for cross-sectional HIV-1 subtyping data of samples collected between 2000 and 2007. The Medline literature database was searched for HIV-1 subtyping data for each country using the terms "HIV", "subtype" and the relevant country names. All potentially relevant articles in English were retrieved and HIV-1 subtyping data from samples collected between 2000–2007 were included in our study. Data submitted to us and derived from the literature were combined to determine the overall proportions of HIV-1 subtypes and recombinants in each country. In addition to information on HIV-1 subtypes, the data sets included country (and region/city) of sample origin, sampling year, transmission route/risk group, detection method, and the genome segment(s) analysed. Overall, subtyping data of 41.8% of the samples originated from previously unpublished data by members of the WHO-UNAIDS Network for HIV Isolation and Characterisation, 35.6% were derived from the published literature, and 22.6% were both submitted to us and published.

Global HIV-1 epidemiology and regional country groupings

Country-specific HIV-1 epidemiology data were obtained from the UNAIDS/WHO estimates of the burden of HIV-1 in the years 2000 through 2007 [26]. For each country the average number of HIV-1 infections in the periods of 2000–2003 and 2004–2007 was determined and used in further analysis.

Countries were grouped in geographical regions according to the UNAIDS classification [26], with some modifications. Sub-Saharan Africa was divided into five separate regions (West, East, Central and Southern Africa, and Ethiopia), because the region has the largest number of HIV-1 infections and a high level of regional HIV-1 subtype diversity. India and Ethiopia were analysed separately as most infections were caused by a single subtype (C), which would have skewed the distribution in their respective regions, where other subtypes predominate. These modifications resulted in the final grouping of all countries into 15 regions, as specified in the legend of Table 2.

Data analysis

The HIV-1 subtype distribution in each region was determined by first multiplying the proportions of all subtypes and recombinants in each country in each period (2000–2003 or 2004–2007) by the estimated (average) number of people living with HIV in the same country in the relevant period. The resulting numbers of each subtype in each country in each region were added up and used to calculate the proportions of the different subtypes and recombinants in each region. Countries for which no HIV-1 subtyping data had been obtained were not included in this part of the analysis.

To determine the global distribution of HIV-1 variants, the regional proportions of HIV-1 subtypes and recombinants were multiplied by the number of HIV-1 infected individuals in each region (including countries for which no subtyping data were obtained). The resulting total numbers of people living with each subtype in each region were added up and the global distribution of HIV-1 subtypes and recombinants was derived.

To determine the spread over the regions of individual subtypes, the estimated number of infections caused by a subtype in each region was taken as a proportion of the global number of infections caused by that same subtype.

Results

Primary HIV-1 subtype distribution data

HIV-1 subtype characterisation data were collected from a total of 65913 samples from HIV-infected individuals in 109 countries between 2000 and 2007. For our analysis the data were divided into two time periods (2000–2003 and 2004–2007) and 15 geographical regions (Methods, Table1, legend to Table2). In 2000–2003, 39148 samples from 95 countries were analysed, and in 2004–2007, 26765 samples from 70 countries were available.

Worldwide the countries for which HIV-1 subtype distribution data were collected accounted for 94% and 90% of individuals living with HIV-1 in 2000–2003 and 2004–2007, respectively (Table1, last column). In nine out of the 15 regions, for both time periods, the countries with subtype data represented more than 90% of people living with HIV in the region.

The number of samples analysed as a proportion of the number of people living with HIV was higher in 2000–2003 than 2004–2007 globally as well as in all but two regions (Table1, 3rd last column). The proportion of the infected population sampled varied between regions and was higher in the Americas, Western and Central Europe, East Asia, and Oceania, whereas India, Middle East & North Africa, and sub-Saharan Africa were less well represented.

Global distribution of HIV-1 subtypes and recombinants

The distribution of HIV-1 subtypes in individual countries was weighted according to the number of HIV-infected people in each country to generate estimates of regional and global HIV-1 subtype distribution for the 2000–2003 and 2004–2007 (Figure1,Table2A). In 2004–2007 subtype C accounted for nearly half (48%) of all global infections. Subtypes A and B caused 12% and 11% of infections, respectively, followed by CRF02_AG (8%), CRF01_AE (5%), subtype G (5%) and D (2%). Subtypes F, H, J and K together caused fewer than 1% of infections worldwide. Other CRFs and URFs are each responsible for 4% of global infections, bringing the combined total of worldwide CRFs (CRF01_AE, CRF02_AG, CRF03_AB and other CRFs) to 16% and all recombinants (all CRFs and URFs) to over 20% (Figure1,Table2A).

Overall, the global distributions of subtypes were similar between 2000–2003 and 2004–2007 and in line with previous estimates [4, 6, 25]. Three epidemiological trends were noted (Table2A). Firstly, an increase in the global proportion (and absolute growth) of the epidemics of subtypes A, F, G, H, CRF01_AE, CRF02_AG and other CRFs was observed. Secondly, the epidemics caused by subtypes D, J, K, CRF03_AB and URFs decreased in size and thus their proportion of the global total became smaller. Thirdly, the epidemics caused by subtypes B and C grew at a rate below the average, resulting in a decrease of their proportion of the global epidemic, though subtype C still caused the largest absolute increase in number of infections.

The global proportion of all CRFs combined increased by 4.5%, which corresponds to a 50% increase in the number of infections. In contrast, the proportion of infections caused by URFs diminished by 3.1%, a 39% decrease of the burden of URFs. Together, all recombinants (CRFs & URFs) increased by 17%, resulting in a 1.4% increase in the proportion of recombinant infections to a total of 20.5% (Table2A). These changes reflect a widespread trend, as an increase in the proportion of other CRFs and a decrease in URFs is widely observed in 10 of the 15 regions (Table2B). It is further notable that, among the major subtypes, subtype A increased and subtype D decreased globally (Table2A).

Regional distribution of HIV-1 subtypes and recombinants

The distribution of HIV-1 subtypes and recombinants in each region is strikingly different across the world (Figure2, Table2B, and Supplemental Digital Content 1, which shows the subtype distribution in individual countries in 2000–2003 and 2004–2007). Changes in regional subtype distributions are shown in table 2B. The regional subtype distributions in 2004–2007 are discussed here.

The greatest diversity is found in Central Africa where all subtypes and many CRFs and URFs are represented (Figure2, Table2B, and SDC1). The six countries in this region all harbour a great subtype diversity, but differ in the dominant subtypes (see SDC1). In the Democratic Republic of the Congo all subtypes, CRF01_AE, CRF02_AG and many other CRFs and URFs are found, except subtype B (see SDC1).

In West Africa all subtypes are detected with the dominant variants being CRF02_AG and subtype G. In East Africa the majority of infections are due to subtype A, with the remainder due to subtypes C and D, and URFs. In Southern Africa, Ethiopia and India the epidemics are nearly exclusively caused by subtype C.

Subtype B dominates in North America, the Caribbean, Latin America, Western and Central Europe and Australia. In Western and Central Europe all major subtypes and many CRFs and URFs are detected. The epidemic in Eastern Europe and Central Asia is dominated by subtype A and subtype B.

In South and South-East Asia CRF01_AE is responsible for the vast majority of infections. In this region the combined proportion of all recombinant infections is 86%, which is the highest in the world. In East Asia the epidemic is dominated by CRF07_BC & CRF08_BC, CRF01_AE, and subtype B. The Middle East and North Africa is mainly affected by subtype B and various CRFs.

Global spread of individual HIV-1 subtypes and recombinants

The distribution of individual HIV-1 subtypes and recombinants across the globe is shown in Figure3 and Supplemental Digital Content 2 and 3. The majority of global dominant subtype C is present in Southern Africa and India, with further infections in East Africa and Ethiopia (Table2). Subtype A is mainly found in East Africa and Eastern Europe & Central Asia, with the remainder in West and Central Africa and South & South-East Asia. The subtype B epidemic is more widely and evenly spread than the other subtypes. For eight subtypes/CRFs analysed 95% of infections are contained in only three or fewer regions. In contrast, 95% of subtype B is spread over 7 regions (Figure3, SDC2&3). Interestingly, hardly any subtype B infections are found in sub-Saharan Africa.

CRF02_AG is the fourth largest variant globally and is concentrated in West Africa, with smaller numbers in Central Africa and the Middle East & North Africa. CRF01_AE is the fifth largest subtype and is found in South & South-East Asia, East Asia and a small number in Central Africa.

Subtype G is concentrated in West and Central Africa. Subtype D is present mainly in Eastern Africa, with further infections in Central and West Africa. Subtype F is widely and evenly spread worldwide, whereas subtype H, J and K are found in Central, Southern and West Africa. CRF03_AB does not play a significant role globally or regionally.

Other CRFs are differentially distributed over West Africa (mainly CRF06_cpx), East Asia (mainly CRF07_BC & CRF08_BC in China), Central Africa (CRF11_cpx among others), Latin America (CRF12_BF, CRF28_BF, CRF31_BC, CRF38_BF, and others), Middle East

& North Africa (mainly CRF06_cpx), and South & South-East Asia (mainly CRF35_AD and CRF07_BC). A wide variety of URFs is distributed over sub-Saharan Africa, Latin America (mainly unique BF recombinants) and South and South-East Africa.

Discussion

The global distribution of HIV-1 subtypes was broadly stable over the 2000–2007 period, with an overall increase in recombinants (Figure1,Table2A) and dynamic changes in some regions (Figure2, Table2B, SDC1). The global HIV subtype distribution was broadly similar to estimated distributions obtained using published data only, as well as estimates calculated by combining country HIV subtype distributions in the Los Alamos database with the country-specific numbers of HIV-infected people used in our study [4, 6, 25](data not shown). The observed trends in subtype distribution between the periods were caused by an interplay between changes in subtype distribution in countries and in the numbers of HIV-infected people (Tables1&2, SDC1). These changes over an 8-year period are consistent with a stabilising global epidemic with a significant annual turnover due to new infections and deaths, and rapid growth of certain regional epidemics (Table1)[1].

Our study has some limitations. Some regions had poor coverage because of lack of data (Caribbean, Oceania, Middle East and North Africa; Table 1, last column), some countries and regions had small sample sizes, in particular those which harbour the largest number of infections and have the highest subtype diversity (Table1), and only a small amount of data were obtained from representative national surveys. Moreover, the heterogeneous nature of the data sets from the two time periods precluded a direct comparison and statistical analysis. Sampling biases may have occurred due to patient selection (risk groups, treatment failure, disease progression), limited geographical coverage and consistency within countries, and unknown dates and places of infection. In addition, subtyping methods used and the type and number of genome segments analysed may have affected results. Finally, publication bias may have occurred in the data derived from the literature.

We found a notable increase in the proportion of CRFs, a decrease in URFs and an overall increase in recombinants, although no formal statistical test for trend was used (Table2A). Detailed examination showed that these trends could not be attributed to the subtyping methods used or the type and number of genome segments analysed in the different periods (data not shown). However, given the relatively recent establishment of rules governing CRF nomenclature [5], samples with discordant subtypes in different genome segments may have been classified as recombinants (or URFs), before the relevant CRFs were characterised, especially in the earlier time period. It is probable that the overall proportion of recombinants is underestimated in both periods due to the limited number of full-length sequences available (0.6–5%; data not shown).

Independent studies in Uganda, Tanzania and Kenya suggest that subtype D infection is associated with faster disease progression than subtype A in populations where they co-circulate, despite similar plasma viral loads [11–13]. In addition, a higher rate of heterosexual transmission of subtype A than subtype D was reported [14]. A long term study examining the subtype distribution in Kenya during the expanding epidemic found a significant decrease in the proportion of subtype D and a slight increase in subtype A [27]. These reports are consistent with our findings of an increase in the proportion of subtype A and a decrease in subtype D in East Africa and globally.

The explanations for the current global subtype distribution and the recent changes observed are probably multifactorial and include founder effects, population growth and urbanisation, and improved transport links and migration [3, 28]. It is uncertain at present whether

biological properties of different subtypes and recombinants play a role in their differential spread.

HIV diversity, in populations and in individuals, is one of the major challenges in HIV vaccine development. It seems clear that vaccine immunogen sequence should match as closely as possible the viral sequences circulating in the target population. Up to date and accurate information on HIV subtype distribution is therefore essential, not least to ensure that efforts and funding are allocated according to the regional and global impact of the various HIV subtypes and recombinants. Our study highlights that the distribution of subtypes and recombinants globally and regionally is extremely complex. This diversity may be addressed by the use of consensus, ancestral, centre-of-tree or mosaic sequences in vaccines [21, 29].

The challenges posed by the genetic diversity of the HIV-1 pandemic to prevention and treatment efforts demand that global molecular epidemiology surveillance is continued and improved. In particular, full length sequencing of samples obtained from nationally representative surveys, taking account of geographical differences and differences in transmission routes/risk groups, are urgently needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Appendix

Contributing members of the WHO/UNAIDS Network for HIV Isolation and Characterisation [name of contributor (country where contributor is based)]: S. Agwale (Nigeria), J-P. Allain & L. Fischetti (UK), C. Archibald, J Brooks & M. Ofner (Canada), E. Belabbes (Algeria), J. Brandful (Ghana), M. Bruckova & M. Linka (Czech Republic), F. Buonaguro & L. Buonaguro (Italy), J. Carr (USA), D. Cooper, T. Kelleher, A. Carrera & P. Cunningham (Australia), D. Dwyer & F. Raikanikoda (Australia), B. Ensoli & S. Butto (Italy), M. Essex & V. Novitsky (USA), H. Fleury (France), F. Gao (USA), G-M. Gershy-Damet (Zimbabwe), Z. Grossman & S. Maayan (Israel), X. He (China), D. Ho & L. Zhang (USA), M. Hoelscher (Germany), M. Hosseinipour & J. van Oosterhout (Malawi), P. Kaleebu & R. Goodall (Uganda), M. Kalish (USA), P. Kanki (USA), E. Karamov (Russian Federation), D. Kombate-Noudjo & A. Dagnra (Togo), T. Leitner (USA), I. Lorenzana de Rivera (Honduras), F. McCutchan (USA), F. Mhalu, W. Urassa, F. Mosha & D. Mloka (Tanzania), M. Morgado (Brazil), J. Mullins, M. Campbell, C. Rousseau, J. Herbeck & M. Rolland (USA), J. Najera & M. Thomson (Spain), P. Nyambi (USA), A. Papa (Greece), J. Pape & C. Nolte (Haiti), M. Peeters (France), J-M. Reynes (Cambodia), M. Salminen (Finland), H. Salomon & M. Carillo (Argentina), B. Schroeder (New Zealand), M. Segondy

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Composition of regions

Countries are underlined if HIV-1 subtype distribution data was obtained for the period 2000–2003 (hatched; ̱), 2004–2007 (single underlined; ̲), or both 2000–2003 & 2004–2007 (double underlined; ̲).

North America: Canada, USA;

Caribbean: Bahamas, Barbados, Cuba, Dominican Republic, Haiti, Jamaica, Trinidad and Tobago;

Latin America: Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, Venezuela;

Western and Central Europe: Albania, Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Montenegro, Netherlands, Norway, Poland, Portugal, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, The Former Yugoslav Republic Macedonia, the United Kingdom;

Eastern Europe and Central Asia: Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Bulgaria, Croatia, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkmenistan, Ukraine, Uzbekistan; *India*

South and South-East Asia (excl. India): Afghanistan, Bangladesh, Bhutan, Brunei Darussalam, Cambodia, Indonesia, Iran (Islamic Republic of), Lao People's Democratic Republic, Malaysia, Maldives, Myanmar, Nepal, Pakistan, Philippines, Singapore, Sri Lanka, Thailand, Timor-Leste, Viet Nam;

East Asia: China, Democratic People's Republic of Korea, Japan, Mongolia, Republic of Korea;

Oceania: Australia, Fiji, New Zealand, Papua New Guinea;

Middle East and North Africa: Algeria, Bahrain, Cyprus, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Qatar, Saudi Arabia, Sudan, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen;

West Africa: Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Equatorial Guinea, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo;

East Africa (excl. Ethiopia): Burundi, Djibouti, Eritrea, Kenya, Mauritius, Rwanda, Somalia, Uganda, United Republic of Tanzania; *Ethiopia*;

Central Africa: Angola, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Gabon;

Southern Africa: Botswana, Comoros, Lesotho, Madagascar, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia, Zimbabwe.

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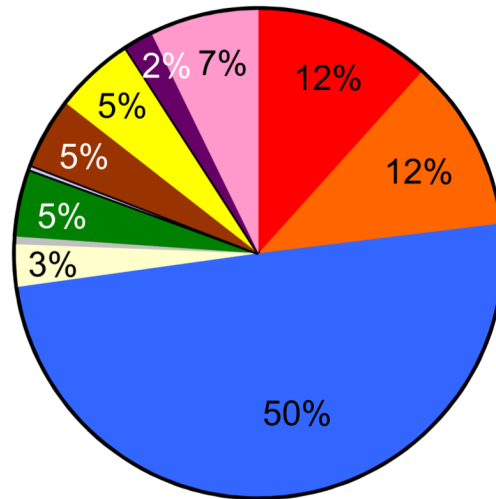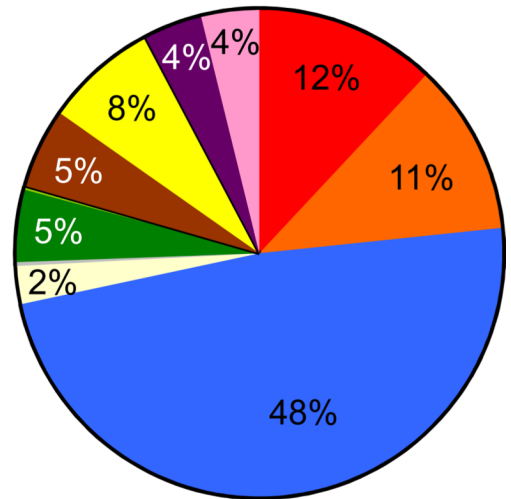
Figure 1. Global distribution of HIV-1 subtypes and recombinants in 2000–2003 and 2004–2007
The number of infections caused by HIV-1 subtypes and recombinants are represented as a proportion of the global total number of people living with HIV-1 in 2000–2003 (A.) and 2004–2007 (B.) (see Table 2A). The colours representing the different HIV-1 subtypes are indicated in the legend on the left-hand side of the figure.

A. **2000-2003**

B. **2004-2007**

Legend:
- A
- B
- C
- D
- F
- G
- H
- J
- K
- CRF01_AE
- CRF02_AG
- CRF03_AB
- Other CRFs
- URFs
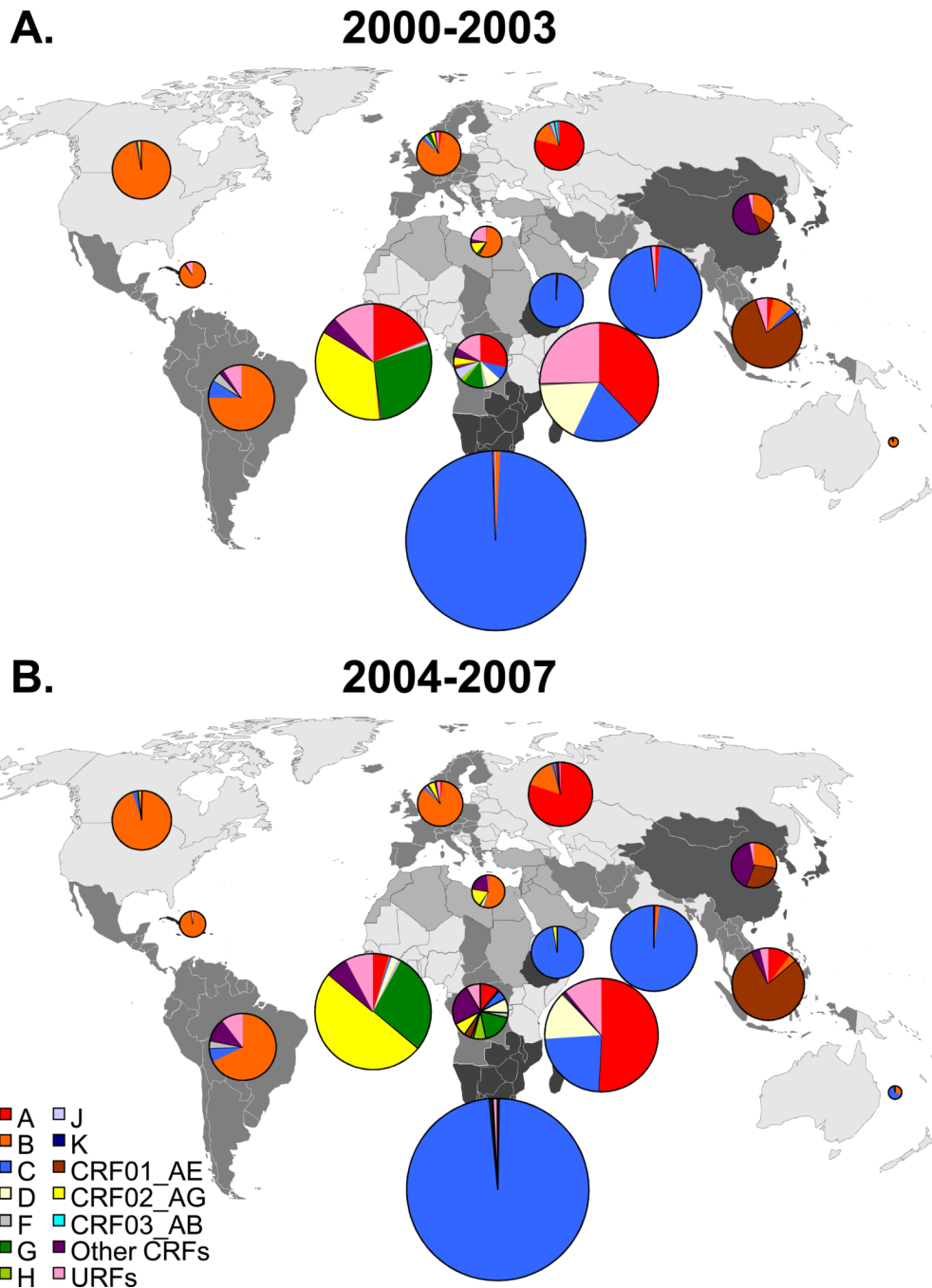
Figure 2. Regional distribution of HIV-1 subtypes and recombinants in 2000–2003 and 2004–2007

The world was divided into 15 regions consisting of groups of countries as specified in the Methods. Countries forming a region are shaded in the same colour. Pie-charts representing the distribution of HIV-1 subtypes and recombinants in each region in 2000–2003 (A.) and 2004–2007 (B.) are superimposed on the regions. The pie-charts were prepared using the data presented in Table 2B. The colours representing the different HIV-1 subtypes are indicated in the legend on the left-hand side of the figure. The relative *surface areas* of the pie-charts correspond to the relative numbers of people living with HIV in the regions (Table 1).

Disclaimer: The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organisation or the Joint United Nations Programme on HIV/AIDS (UNAIDS) concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate borderlines for which there may not yet be full agreement.
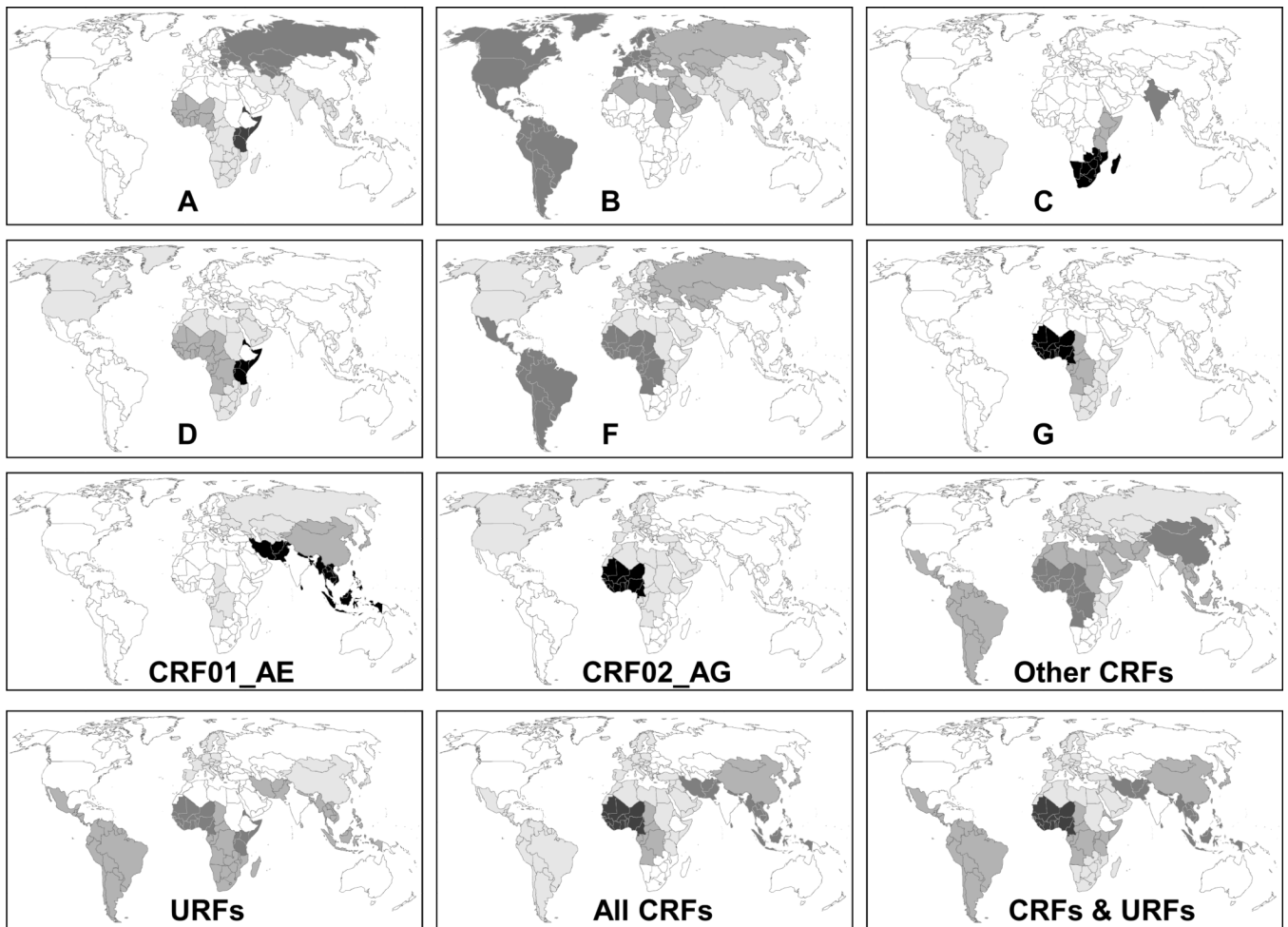
Figure 3. Global distribution of individual HIV-1 subtypes and recombinants in 2004–2007
For each subtype/recombinant indicated each of the 15 regions is shaded according to the proportion of the global number of infections caused by the subtype/recombinant present in each region.

■ 70-100 %

■ 40-70 %

■ 15-40 %

■ 5-15 %

□ 0.5-5 %

□ < 0.5 %
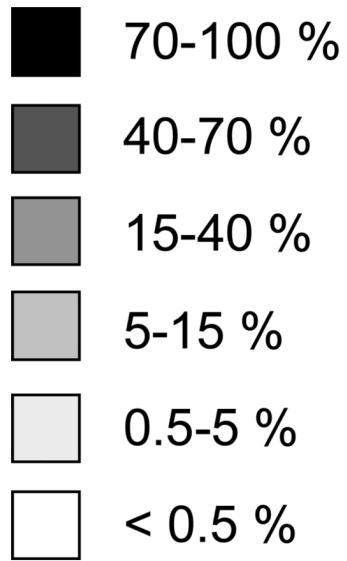
Percentage of global total

Table 1

Global and regional HIV-1 epidemiology and sample collection

Region of the world	Number of individuals living with HIV (n) [a]		HIV infections as a proportion of global total (%) [b]		Change in the number of HIV infections (%) [c]	Number of samples collected (n)		Depth of sampling (%) [d]		Number of countries with HIV-1 subtype data (n) [e]		Coverage of region (%) [f]	
	2000–2003	2004–2007	2000–2003	2004–2007		2000–2003	2004–2007	2000–2003	2004–2007	2000–2003	2004–2007	2000–2003	2004–2007
North America	1100000	1200000	3.6	3.6	11.0	2097	4117	0.195	0.346	2	2	100.0	100.0
Caribbean	210000	230000	0.7	0.7	9.1	539	56	0.258	0.025	4	4	39.2	90.9
Latin America	1400000	1500000	4.6	4.7	10.7	5395	3899	0.392	0.256	13	7	77.9	75.2
Western and Central Europe	620000	700000	2.1	2.1	13.2	14108	7334	2.278	1.046	16	8	88.3	69.6
Eastern Europe and Central Asia	780000	1400000	2.6	4.3	81.1	2071	623	0.267	0.044	11	5	98.8	67.0
India	2700000	2500000	9.0	7.6	−7.4	685	449	0.025	0.018	1	1	100.0	100.0
South and South-East Asia (excl. India)	1600000	1800000	5.2	5.4	13.1	2137	2084	0.136	0.117	8	7	84.6	67.3
East Asia	510000	690000	1.7	2.1	34.7	1972	2142	0.384	0.310	3	3	100.0	99.9
Oceania	28000	57000	0.1	0.2	105.2	906	1105	3.286	1.953	2	3	56.1	97.7
Middle East and North Africa	310000	360000	1.0	1.1	16.2	283	363	0.091	0.101	5	3	4.1	5.5
West Africa	4200000	4600000	14.1	14.0	7.7	3252	1398	0.077	0.031	10	7	94.0	87.2
East Africa (excl. Ethiopia)	4400000	4400000	14.6	13.5	0.2	3098	2002	0.071	0.046	6	4	98.9	95.5
Ethiopia	920000	930000	3.1	2.8	0.3	235	39	0.025	0.004	1	1	100.0	100.0
Central Africa	910000	1100000	3.0	3.3	17.1	979	388	0.107	0.036	6	6	100.0	100.0
Southern Africa	10000000	11000000	34.5	34.6	9.0	1391	766	0.013	0.007	7	9	96.0	96.0
Global	30000000	33000000	100.0	100.0	9.0	39148	26765	0.130	0.082	95	70	94.0	90.1

[a] The numbers of individuals living with HIV were obtained from the UNAIDS/WHO estimates of the burden of HIV[26]. The average of the numbers of infections in the periods 2000–2003 and 2004–2007 are shown. Figures are rounded off.

[b] The numbers of individuals living with HIV in each region as a proportion of the global total, based on the averages of the numbers of infections in each period (%).

[c] The change in the number of HIV infections between the periods 2000–2003 and 2004–2007 as a proportion of the number of infections in 2000–2003 (%).

[d] The number of samples collected from a region as a proportion of the number of people living with HIV in the region (%).

[e] Countries for which HIV subtype data was collected are specified in the legend of Table 2.

[f] The combined number of people living with HIV in the countries for which HIV subtype distribution data were collected in a region (see legend of Table 2), as a proportion of the total number of people living with HIV in the region. If any data was available for a country (independent of the number of samples collected), the whole HIV-infected population in that country was deemed to be represented in this analysis.

Table 2

Distribution of HIV-1 subtypes and recombinants globally (A.) and in each region (B.) in 2000–2003 and 2004–2007

Proportions of HIV-1 subtypes and recombinants in each region and the world (%). The countries making up each region are specified below.

A.

Year	A	B	C	D	F	G	H	J	K	CRF01_AE	CRF02_AG	CRF03_AB	Other CRFs [a]	URFs [b]	Total CRFs [c]	Total CRFs & URFs [d]
2000–2003 [e]	11.56	11.57	49.62	2.87	0.44	4.50	0.10	0.24	0.02	4.52	5.45	0.04	1.96	7.12	11.96	19.08
2004–2007 [e]	12.03	11.33	48.23	2.49	0.45	4.60	0.26	0.12	0.01	5.09	7.73	0.00	3.65	4.01	16.47	20.48
Change [f]	0.47	−0.23	−1.40	−0.37	0.02	0.10	0.16	−0.12	−0.01	0.57	2.28	−0.04	1.69	−3.11	4.51	1.40
Global																
2000–2003 [g]	3500000	3500000	14900000	860000	130000	1400000	29000	71000	7100	1400000	1600000	12000	590000	2100000	3600000	5700000
2004–2007 [g]	3900000	3700000	15800000	820000	150000	1500000	85000	38000	3400	1700000	2500000	100	1200000	1300000	5400000	6700000
Change [h]	13.4	6.8	5.9	−5.3	13.0	11.3	191.9	−46.4	−52.3	22.7	54.7	−99.3	103.4	−38.7	50.0	16.9

B.

Region of the world	Year [i]	A	B	C	D	F	G	H	J	K	CRF01_AE	CRF02_AG	CRF03_AB	Other CRFs [a]	URFs [b]	Total CRFs [c]	Total CRFs & URFs [d]
North America	2000–2003	0.88	95.55	1.08	0.01	0.00	0.00	0.00	0.00	0.00	0.49	1.73	0.00	0.00	0.26	2.22	2.48
	2004–2007	0.70	94.20	2.46	0.45	0.10	0.20	0.01	0.00	0.00	0.43	1.44	0.00	0.01	0.02	1.87	1.89
	Change	−0.18	−1.35	1.38	0.45	0.10	0.20	0.01	0.00	0.00	−0.06	−0.30	0.00	0.01	−0.24	−0.36	−0.59
Caribbean	2000–2003	0.03	89.67	0.28	0.00	0.01	0.13	0.01	0.00	0.00	0.00	0.02	0.00	1.22	8.64	1.25	9.50
	2004–2007	0.00	98.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.68	0.00	1.68
	Change	−0.03	8.66	−0.28	0.00	−0.01	−0.13	−0.01	0.00	0.00	0.00	−0.02	0.00	−1.22	−6.96	−1.25	−7.83
Latin America	2000–2003	0.00	74.90	8.99	0.06	4.69	0.00	0.00	0.00	0.00	0.00	0.03	0.00	2.29	9.04	2.32	11.36
	2004–2007	0.00	67.89	6.53	0.04	3.53	0.00	0.00	0.00	0.00	0.01	0.04	0.00	11.29	10.67	11.34	22.01
	Change	0.00	−7.01	−2.46	−0.02	−1.16	0.00	0.00	0.00	0.00	0.01	0.01	0.00	9.01	1.63	9.02	10.65
Western and Central Europe	2000–2003	2.22	84.13	2.90	0.73	0.41	2.82	0.06	0.10	0.02	0.79	2.94	0.01	1.00	1.88	4.73	6.61
	2004–2007	1.76	85.20	1.91	0.27	0.47	1.00	0.07	0.00	0.00	1.01	4.50	0.00	1.22	2.57	6.73	9.30
	Change	−0.45	1.07	−0.99	−0.46	0.07	−1.82	0.02	−0.10	−0.02	0.22	1.56	−0.01	0.22	0.69	2.00	2.69
Eastern Europe and Central Asia	2000–2003	78.81	14.09	1.19	0.26	2.45	0.26	0.00	0.00	0.00	0.26	0.05	1.55	0.48	0.60	2.34	2.95
	2004–2007	80.01	15.20	1.51	0.00	1.14	0.01	0.00	0.00	0.00	0.76	0.01	0.01	0.92	0.44	1.69	2.13

B.

Region of the world	Year[i]	A	B	C	D	F	G	H	J	K	CRF01_AE	CRF02_AG	CRF03_AB	Other CRFs[a]	URFs[b]	Total CRFs[c]	Total CRFs & URFs[d]
	Change	1.20	1.12	0.32	−0.26	−1.31	−0.25	0.00	0.00	0.00	0.50	−0.04	−1.55	0.43	−0.16	−0.65	−0.82
India	2000–2003	1.40	0.31	96.54	0.00	0.00	0.00	0.00	0.00	0.00	0.36	0.00	0.00	0.10	1.29	0.47	1.76
	2004–2007	0.89	1.34	97.77	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Change	−0.50	1.03	1.23	0.00	0.00	0.00	0.00	0.00	0.00	−0.36	0.00	0.00	−0.10	−1.29	−0.47	−1.76
South and South-East Asia (excl. India)	2000–2003	2.89	9.12	3.03	0.01	0.00	0.03	0.00	0.00	0.00	79.57	0.01	0.00	0.31	5.03	79.89	84.92
	2004–2007	10.24	3.62	0.04	0.00	0.00	0.00	0.00	0.00	0.00	78.60	0.05	0.00	3.70	3.74	82.35	86.10
	Change	7.35	−5.49	−2.99	−0.01	0.00	−0.03	0.00	0.00	0.00	−0.97	0.04	0.00	3.39	−1.29	2.46	1.18
East Asia	2000–2003	0.66	33.06	0.08	0.00	0.00	0.05	0.00	0.00	0.00	10.58	0.11	0.00	51.53	3.93	62.22	66.15
	2004–2007	0.24	26.17	1.38	0.00	0.01	0.06	0.00	0.00	0.00	27.62	0.46	0.00	40.89	3.19	68.96	72.15
	Change	−0.43	−6.89	1.30	0.00	0.01	0.01	0.00	0.00	0.00	17.04	0.35	0.00	−10.64	−0.75	6.74	6.00
Oceania	2000–2003	0.51	87.62	5.19	0.54	0.11	0.00	0.00	0.00	0.00	4.39	1.25	0.00	0.21	0.17	5.85	6.02
	2004–2007	0.24	31.17	66.34	0.00	0.06	0.09	0.00	0.00	0.00	1.24	0.53	0.00	0.00	0.33	1.78	2.10
	Change	−0.27	−56.45	61.15	−0.54	−0.05	0.09	0.00	0.00	0.00	−3.15	−0.72	0.00	−0.21	0.16	−4.08	−3.92
Middle East and North Africa	2000–2003	0.76	57.25	0.00	0.76	0.00	2.29	0.00	0.00	0.00	0.00	12.98	0.00	3.82	22.14	16.79	38.93
	2004–2007	0.98	53.59	0.45	2.23	0.37	1.84	0.00	0.00	0.00	0.02	18.08	0.00	21.34	1.10	39.45	40.55
	Change	0.21	−3.67	0.45	1.46	0.37	−0.45	0.00	0.00	0.00	0.02	5.11	0.00	17.53	−21.03	22.65	1.62
West Africa	2000–2003	18.73	0.02	0.38	0.45	0.32	27.87	0.06	0.21	0.01	0.35	35.23	0.00	4.79	11.59	40.37	51.96
	2004–2007	4.36	0.35	0.66	1.87	0.84	27.59	0.12	0.15	0.06	0.07	50.07	0.00	6.20	7.66	56.34	64.00
	Change	−14.37	0.32	0.28	1.42	0.52	−0.28	0.06	−0.05	0.05	−0.28	14.84	0.00	1.41	−3.93	15.97	12.04
East Africa (excl. Ethiopia)	2000–2003	38.00	0.05	19.08	16.89	0.05	0.37	0.00	0.00	0.00	0.00	0.17	0.00	0.12	25.28	0.29	25.57
	2004–2007	50.80	0.01	22.97	13.80	0.11	0.29	0.00	0.00	0.00	0.17	0.22	0.00	0.72	10.90	1.12	12.02
	Change	12.80	−0.03	3.89	−3.08	0.07	−0.08	0.00	0.00	0.00	0.17	0.06	0.00	0.60	−14.38	0.83	−13.55
Ethiopia	2000–2003	1.28	0.00	98.30	0.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	2004–2007	0.00	0.00	97.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.56	0.00	0.00	0.00	2.56	2.56
	Change	−1.28	0.00	−0.86	−0.43	0.00	0.00	0.00	0.00	0.00	0.00	2.56	0.00	0.00	0.00	2.56	2.56
Central Africa	2000–2003	28.74	0.14	7.98	8.81	2.45	12.35	2.90	6.73	0.72	1.69	5.15	0.00	5.54	16.78	12.38	29.17
	2004–2007	11.15	0.53	5.75	8.51	2.69	18.17	7.41	1.39	0.07	4.07	7.86	0.00	24.03	8.39	35.96	44.34

B.

Region of the world	Year[i]	A	B	C	D	F	G	H	J	K	CRF01_AE	CRF02_AG	CRF03_AB	Other CRFs[a]	URFs[b]	Total CRFs[c]	Total CRFs & URFs[d]
	Change	−17.59	0.39	−2.24	−0.30	0.23	5.82	4.51	−5.35	−0.66	2.37	2.71	0.00	18.49	−8.40	23.57	15.18
Southern Africa	2000–2003	0.06	0.69	98.77	0.06	0.06	0.12	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.17	0.06	0.23
	2004–2007	0.21	0.04	98.31	0.14	0.00	0.17	0.00	0.14	0.00	0.00	0.02	0.00	0.02	0.95	0.05	0.99
	Change	0.14	−0.65	−0.46	0.08	−0.06	0.05	0.00	0.14	0.00	0.00	−0.04	0.00	0.02	0.78	−0.02	0.76

[a] Circulating Recombinant Forms (CRFs) other than CRF01_AE, CRF02_AE and CRF03_AB.

[b] Unique Recombinant Forms (URFs).

[c] The combined proportions of CRF01_AE, CRF02_AE, CRF03_AB, and other CRFs.

[d] The combined proportions of all CRFs (see c) and URFs (see b).

[e] Global proportions of HIV-1 subtypes and recombinants are presented for the periods indicated (%).

[f] Global changes between the two periods in the proportions of each subtype/recombinant (percentage points).

[g] The global number of infections caused by each subtype/recombinant in the periods indicated. Figures are rounded off.

[h] Changes between the two periods in the global numbers of each subtype/recombinant (%).

[i] Proportions of HIV-1 subtypes and recombinants are presented for each region for the periods indicated. Changes between the two periods in the proportions of each subtype in each region (percentage points).